

# SOLID-PHASE SYNTHESIS OF AMMONIUM IONENES<sup>†</sup>

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## Introduction

Ionenes are a class of polyelectrolytes containing ionic charges within the polymer backbone.<sup>1</sup> Figure 1 shows the structure of an ammonium ionene synthesized from 1,6-dibromohexane and *N,N,N',N'*-tetramethyl-1,6-diaminohexane. Because each repeat unit contains a specific number of ionic charges, the charge density along the ionene backbone can be precisely controlled. This well-defined ionic structure enables ionenes to act as physical crosslinkers for high performance elastomeric films.<sup>1</sup> Ionenes also bind strongly with oppositely-charged polyelectrolytes for applications including gene transfection and heparin binding.<sup>2,3</sup>

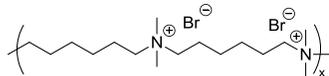


Figure 1. Structure of a 6,6 ammonium ionene.

Solid-supported polymerization methods have become popular with the advent of solid-phase peptide synthesis (SPPS).<sup>4</sup> The advantages of solid-phase synthesis include precise control over molecular weight and monomer sequence, ease of automation, and the ability to incorporate non-natural amino acid monomers. More recently, brush polymers have seen intense research interest as a technique to introduce specific surface chemistries and stimuli-responsive attributes to the surface of nanoparticles, microfluidic channels, and porous membranes, among others.<sup>5</sup>

The formation of polyelectrolyte complexes depends on the molecular weight of the polycation and polyanion.<sup>6</sup> However, synthetic parameters (including using endcapping agents and controlling monomer stoichiometry) only provide rough control over ionene molecular masses. In this work, model surfaces were designed for the solid-supported synthesis of ammonium ionenes. Quantitative X-ray photoelectron spectroscopy (XPS) allowed us to identify ideal reaction conditions and monitor the polymerization of ionenes from the surface of silicon wafers.

## Experimental

**Materials.** Acetonitrile, toluene, 1,6-dibromohexane, and *N,N,N',N'*-tetramethyl-1,6-diaminohexane were obtained from Sigma-Aldrich<sup>‡</sup> and distilled from CaH<sub>2</sub> prior to use. 3-(*N,N*-dimethylamino)propyl-trimethoxysilane was obtained from Gelest and used as received. All other reagents were obtained from commercial sources and used as received.

**Preparation of Amine Monolayer.** Silicon wafers were first cleaned using a solution of 70/30 vol/vol sulfuric acid/hydrogen peroxide (CAUTION: This 'piranha solution' is highly corrosive and should be used with extreme care) and rinsed thoroughly with de-ionized water. The wafers were then submerged in a solution of 20 mmol/L 3-(*N,N*-dimethylamino)propyl-trimethoxysilane in dry toluene overnight. The presence of amine monolayer was confirmed by XPS.

**Preparation of Ionene Surfaces.** Two separate monomer solutions were prepared: 1.0 mol/L 1,6-dibromohexane in acetonitrile (dibromide solution) and 1.0 mol/L *N,N,N',N'*-tetramethyl-1,6-diaminohexane (diamine solution). Both solutions were heated to 50 °C. Amine-functionalized silicon wafers were submerged in the dibromide solution for 45 min. After reaction, the wafers were removed, rinsed thoroughly with acetonitrile, and submerged in the diamine solution. This alternating process was repeated until the desired number of monomers was added.

**X-ray Photoelectron Spectroscopy (XPS).** XPS measurements were performed using a Kratos Axis Ultra Spectrometer (Kratos Analytical, Manchester, UK) with a monochromatic Al K X-ray source (1486.6 eV).

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<sup>‡</sup> Certain commercial equipment, instruments, or materials are identified in this paper in order to specify the experimental procedure adequately. Such identification is not intended to imply recommendation or endorsement by the National Institute of Standards and Technology, nor is it intended to imply that the materials or equipment identified are necessarily the best available for the purpose.

## Results and Discussion

The conventional synthesis of ammonium ionenes is performed in refluxing methanol or acetonitrile for up to 24 h. The formation of high molecular weight polymers in viscous solution requires long reaction times. To identify reaction conditions for solid-phase synthesis, model cationic surfaces were prepared with 6-bromohexanoic acid. The carbonyl carbon of the hexanoic acid provided a tag for XPS analysis. Quantitative XPS analysis indicated the reaction reached quantitative conversion at 45 min. These conditions were used for subsequent reactions.

The synthesis of ionene-functionalized surfaces is shown in Figure 2. The tertiary amine monolayers were reacted successively with dibromide and diamine, then analyzed by XPS following each step to monitor the reaction progress. Quantitative XPS analysis of the C<sub>1s</sub> region indicated incomplete conversion at each reaction step. The first dibromide layer reached 80% conversion. The subsequent reaction with diamine reacted with 40% of the available bromide end groups. The following dibromide and diamine reactions both only reached 20% conversion. As the ionene brushes build up from the dense tertiary amine monolayer, the surface charge density increases dramatically. Presumably, each subsequent reaction becomes hindered by both crowding of the brushes and ionic repulsions between charges.

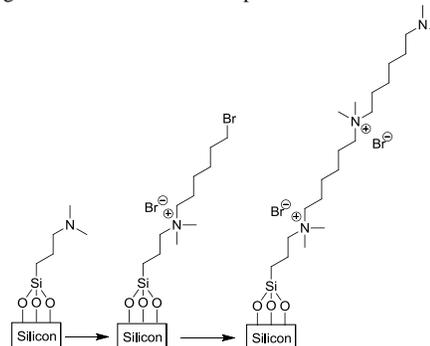


Figure 2. Synthesis of ionene brushes via successive reaction with dibromide and diamine. Only the first two reactions are shown.

Ongoing work focuses on controlling the ionene graft polymerization. Monolayers will be prepared from mixtures of the tertiary amine silane and inert alkyl silane to lower the density of growing ionene chains. This will identify the ideal grafting density for well-controlled brushes. In addition, to determine if any looping reactions are occurring, where one difunctional monomer effectively endcaps two growing chains, the ionenes will be cleaved from the surface for full analysis.

## Conclusions

Ionene brushes were synthesized via solid-phase polymerization from silicon surfaces. Model reactions identified the ideal reaction conditions of 45 min at 50 °C. Preliminary XPS analysis indicated that brush growth does not proceed quantitatively, presumably due to steric and ionic effects in the growing brush layer. This solid-phase synthesis will enable us to prepare ionenes with precisely defined molecular weights, molecular weight distributions, and monomer sequences.

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